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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,749	08/18/2000	MICHAEL S. SU	VPI/97-104 CON	1079

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 03/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/642,749	SU ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): 23.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached office action*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: *11-13*.

   Claim(s) rejected: *10*.

   Claim(s) withdrawn from consideration: *14*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

ADVISORY ACTION

1. The proposed amendments filed on December 15, 2003 have been fully considered but will not be entered because they are not deemed to place the application in better form for appeal by material reducing or simplifying the issues for appeal.

Response to Arguments

In page 6, second paragraph bridging to page 8, last paragraph of applicant's remarks, applicant argues that: (1) "[S]hah does not disclose all the elements of the mutant kinases of claim 10 or 23." since (a) "[S]hah's mutant protein tyrosine kinase, v-Src GST-XIM (V323A, I338A), does not have at least one amino acid substitution in its ATP binding site compared to the naturally-occurring protein kinase. Yet, this element is required by claims 10 (a) and 23 (a).", (b) "[S]hah's mutant kinase does not bind compounds in its ATP binding site with a dissociation constant less than 10 μM. This element is required by claims 10 (b)(i) and 23 (b)(i)."; and (c) "[S]hah does not teach a mutant of a naturally occurring second serine/threonine protein kinase. Shah refers to a mutant of a tyrosine kinase. Claim 23 requires a serine/threonine kinase."; and (2) "[S]hah does not disclose an ATP binding site mutant.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection.

First, regarding claim 10, Shah *et al.*, teach that, in order to form GST-XD4 (V323A, 1338A), two amino acids in the ATP binding site of GST-XD4 are substituted. Since a mutant and a wild type are relative, GST-XD4 is a mutant of GST-XD4 (V323A, 1338A) while GST-XD4 (V323A, 1338A) is a naturally-occurring second tyrosine protein kinase. Claim 10 requires that a mutant has an ATP binding site comprising at least one amino acid substitution compared to an ATP binding site of the naturally-occurring second serine/threonine protein kinase or

tyrosine protein kinase. Since Shah *et al.*, teach that there is at least one amino acid difference in the ATP binding sites between GST-XD4 (V323A, 1338A) and GST-XD4, Shah *et al.*, disclose a mutant (ie., GST-XD4) having an ATP binding site comprising at least one amino acid substitution compared to an ATP binding site of the naturally-occurring second tyrosine protein kinase (ie., GST-XD4 (V323A, 1338A)) as recited in claim 10. Claim 10 also requires that the mutant has an ability to bind to a compound that binds to an ATP binding site of a first serine/threonine protein kinase or first tyrosine protein kinase, wherein said compound is an inhibitor or a ligand of said first serine/threonine protein kinase or said first tyrosine kinase. Since Shah *et al.*, teach that ATP binds the ATP binding site of GST-XD4, Shah *et al.*, disclose a mutant having an ability to bind to a compound (ie., ATP) that binds to an ATP binding site of a first serine/threonine protein kinase or first tyrosine protein kinase (ie., a serine/threonine protein kinase or tyrosine protein kinase) wherein said compound (ie., ATP) is a ligand of said first serine/threonine protein kinase or said first tyrosine kinase as recited in claim 10. Claim 10 also requires that the mutant has a dissociation constant for said inhibitor (Ki) or a dissociation constant for said ligand (Kd) that is less than 10 μM and is at least l0-fold lower than the Ki or Kd of the binding of said compound with said naturally-occurring second serine/threonine protein kinase or second tyrosine protein kinase. Since Shah *et al.*, teach that Km for GST-XD4 binding to ATP is 9-15 μM (12±3) while Km for GST-XD4(V323A, I338A) binding to ATP is 130-170 μM, the dissociation constant of GST-XD4 (ie., a mutant of a naturally-occurring second tyrosine protein kinase) binding to ATP (ie., said compound) is 10-fold lower than dissociation constant of GST-XD4 (V323A, I338A) (ie., a naturally-occurring second tyrosine protein kinase) binding to ATP as recited in claim 10. In other word, GST-XD4 (ie., a mutant of a naturally-occurring tyrosine protein kinase) binding to ATP is much stronger than GST-XD4

(V323A, I338A) (ie., a naturally-occurring second tyrosine protein kinase) binding to ATP. Since Shah *et al.*, teach that Km for GST-XD4 binding to ATP can be 9 μM, the mutant of a naturally-occurring second tyrosine protein kinase (ie., GST-XD4) has a dissociation constant less than 10 μM as recited in claim 10. Therefore, Shah *et al.*, teach all limitations recited in claim 10.

Second, regarding claim 23, claim 23 requires that a mutant has an ATP binding site comprising at least one amino acid substitution compared to an ATP binding site of the naturally-occurring second serine/threonine protein kinase. Since Shah *et al.*, teach a tyrosine kinase, GST-XD4, and it is known in the art that the ATP binding sites of a serine/threonine protein kinase and a tyrosine kinase have at least one amino acid difference, GST-XD4 is a mutant of a naturally occurring second serine/threonine protein kinase having an ATP binding site comprising at least one amino acid substitution compared to an ATP binding site of the naturally occurring second serine/threonine protein kinase (ie., p38) as recited in claim 23. Claim 23 also requires that the mutant has an ability to bind to a compound that binds to an ATP binding site of a first serine/threonine protein kinase, wherein said compound is an inhibitor or a ligand of said first serine/threonine protein kinase. Since Shah *et al.*, teach that ATP binds the ATP binding site of GST-XD4, Shah *et al.*, disclose a mutant having an ability to bind to a compound (ie., ATP) that binds to an ATP binding site of a first serine/threonine protein kinase (ie., a serine/threonine protein kinase) wherein said compound (ie., ATP) is a ligand of said first serine/threonine protein kinase as recited in claim 23. Claim 23 also requires that the mutant has a dissociation constant for said inhibitor (Ki) or a dissociation constant for said ligand (Kd) that is less than 10 μM and is at least 10-fold lower than the Ki or Kd of the binding of said compound with said naturally-occurring second serine/threonine protein kinase. Since Shah *et*

al., teach that Km for GST-XD4 binding to ATP is 9-15 μM (12±3) and according to the specification (see page 28, Table 1), Km for p38 (a naturally occurring second serine/threonine protein kinase) is 260 ±30 μM, Shah *et al.*, disclose that the dissociation constant of GST-XD4 (ie., a mutant of a naturally-occurring serine/threonine protein kinase) binding to ATP (ie., said compound) is 10-fold lower than dissociation constant of p38 (ie., a naturally-occurring second serine/threonine protein kinase) binding to ATP as recited in claim 23. In other word, GST-XD4 (ie., a mutant of a naturally-occurring serine/threonine protein kinase) binding to ATP is much stronger than p38 (ie., a naturally-occurring second serine/threonine protein kinase) binding to ATP. Since Shah *et al.*, teach that Km for GST-XD4 binding to ATP can be 9 μM, the mutant of a naturally-occurring second serine/threonine protein kinase (ie., GST-XD4) has a dissociation constant less than 10 μM as recited in the claim 23. Therefore, Shah *et al.*, teach all limitations recited in claim 23.

2. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
February 24, 2004

BJ FORMAN, PH.D.
PRIMARY EXAMINER